

REMARKS

I. Status of the Claims

Claims 1-3, 5-11, 18-20, 23-25 and 28-32 are pending in the application, and claims 10, 11 and 25 stand withdrawn. Claim 4 has been canceled and claims 12-17, 21, 22, 26 and 27 were previously canceled. Claims 28 -32 are newly added and are supported in the specification in paragraph [0033]. Claims 1, 2, 5, 6, and 18-20 are amended to properly depend from Claim 1 or other dependent claims. Support for the amendment to Claim 1 is found in the specification in paragraph [0030]. Thus, claims 1-3, 5-9, 18-20, 23, 24 and 28-32 are now presented for reconsideration.

Applicants note that the previous rejections under 35 U.S.C. §112, first and second paragraphs, and 35 U.S.C. §103 have been withdrawn by the examiner; however, the examiner has maintained the objections to the declaration and has made a new rejection under 35 U.S.C. §103. Applicants' responses to these specific grounds for objection/rejection are set out in detail below.

II. Objections

The examiner has maintained the objection to the declaration filed on May 26, 2009 and reiterates that a new oath or declaration in compliance with 37 CFR §1.63, including the entire inventive entity remains required. The examiner directs applicants to sections of the MPEP, specifically §201.03 and §605.04. The examiner then states that in order to obviate this issue that it is suggested that the pages of the new oath recite page 1 of 3, page 2 of 3 and page 3 of 3, respectively. Applicants confirm that they did not file a new declaration with the response filed

on September 16, 2009. However, applicants submit that the most recently filed declaration filed on May 26, 2009, meets all of the criteria required by the patent laws and rules.

Applicants specifically direct the examiner to MPEP §605.04(a), I. [second column, first paragraph, page 600-54]. Applicants submit that both sets of declarations, filed in 2007 and again on May 26, 2009, were properly filed according to the rules.

An oath or declaration under 37 CFR 1.63 by each actual inventor must be presented. While each inventor need not execute the same oath or declaration, each oath or declaration executed by an inventor must contain a complete listing of all inventors so as to clearly indicate what each inventor believes to be the appropriate inventive entity. >Where individual declarations are executed, they must be submitted as individual declarations rather than combined into one declaration (by combining the signature pages).

Applicants submitted an oath or declaration signed by each inventor originally in 2007 and again on May 26, 2009. These rules do not set forth the requirement that the declaration use page numbering, such as page 1 of 3, *etc.*, as requested by the examiner. Additionally, the same Word management document number is on each page of each of the declarations filed in 2009 (and also in 2007).

In an effort to clarify this issue, the undersigned attorney spoke to Examiner Duffy on July 11, 2011, regarding this objection, and Examiner Duffy agreed that he would withdraw this objection. The Examiner Interview Summary dated July 21, 2011 confirms that this rejection will be withdrawn. Therefore, it is believed that this objection is moot and that the oath and declaration on file in the present application be accepted and that this objection be withdrawn.

III. Rejections Under 35 U.S.C. §103

Claims 1-9, 18-20, 23 and 24 are rejected as obvious over Kufer *et al.* (WO 98/46645) in view of Raum *et al.* (*Can. Immunol. Immunother.*, 50:141-150, 2001), in view of Naundorf *et al.*

(*Int. J. Can.* 100:101-110, 2002), in view of Korman *et al.*, (US 20020086014, 2002), in view of Wolf *et al.*, (*DDT.*, 7(5):S25-S27, 2002), in view of Raun *et al.*, (*Neoplasia*, 5(6):489-94, 2003), and in view of Leyland-Jones (*J. Clin. Onc.*, 221(21): 3965-3971, 2003). The examiner did not maintain the previous obviousness rejection based on Kufer as the primary reference in combination with secondary references. Therefore, the present obviousness rejection is newly formulated, and the examiner now alleges that the claimed invention would have been *prima facie* obvious to the skilled person absent a showing of unexpected results

Applicants respectfully traverse this rejection because the new combination of the cited prior art also fails to render the presently claimed invention obvious. In support of this traversal, applicants provide a declaration from Dr. Sabine Kaubitzsch. The declaration provides evidence of surprising and unexpected results for the invention as now claimed in a specific cancer expressing the EpCAM antigen – metastatic breast cancer. As explained by the declarant, median time to progression of the disease within the once-every-three-weeks dosing schedule was 165.5 days (95% confidence interval from 42 to 176 days), whereas median time to progression of the disease in the once-weekly dosing schedule was distinctively shorter with 83 days (95% CL from 57 to 124 days).

Based on these data, Dr. Kaubitzsch opines that this study determined that the once-every-three-week dosing schedule provides an improved efficacy over the once-weekly dosing schedule with comparable safety results between the two dosing schedule groups, and further, that this improvement was unexpected. Thus, even if a *prima facie* of obviousness had been made out, these data would effectively rebut it. Not only does the claimed dosing schedule of once-every-three-weeks provide improved and unexpected efficacy as compared to the once-weekly dosing schedule, but the more effective and less frequent once-every-three-week dosing requirement is an advantage for the patients' quality of life by permitting longer times between treatments.

The examiner persists in stating that the MT201 antibody is a therapeutic antibody known in the art and is therefore a variable within the context of MPEP §2144.05. Again, turning to the particular cases cited in support of the rejection, the citation from the *Boesch* case, cited in this section of the MPEP, which actually derives from *In re Antonie*, 195 USPQ 6 (CCPA 1967), is not helpful. The *Boesch* case states that *prima facie* obviousness “may be rebutted where the result of optimizing a variable, which was known to be result effective, are unexpectedly good It is also well settled that proof of unexpected properties may be in the form of direct or indirect comparative testing of the claimed compounds ... and the closest prior art.” That is precisely the case here.

Applicants note that the examiner states on page 13 of the office action:

“...the examiner is not arguing that no dosing regimen would ever be patentable. Indeed if persuasive evidence of unexpected results for a particular dosage amount administered by a particular regimen that treats a specific cancer expressing EpCAM were provided then it might be established that claims drawn to such methods were patentable.”

Applicants submit that just such a situation has been presented here. The present claims require administration of an amount of the antibody and timing sufficient to treat the disease, and further, applicants have provided a declaration by Dr. Kaubitzsch that shows unexpected results of longer time to the progression of the disease in “a specific cancer expressing EpCAM.”

Finally, though the preceding discussion focuses on the issue of unexpected results, applicants wish to reiterate that the claims as now presented for reconsideration describe methodologic aspects of cancer therapy that are neither taught nor suggested by the cited art – namely, a distinct therapeutic regimen that includes a once-every-three-weeks administration. Indeed as opined by Dr. Kaubitzsch, a longer interval therapy would not have been the first choice of the skilled artisan. Again, it does not matter how desirable the *finding* of such

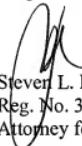
parameters might be. As long as the prior art has not achieved (or suggested) this solution, no *prima facie* case exists.

Therefore, reconsideration and the withdrawal of the rejection based on the preceding comments and attached declaration, is therefore respectfully requested.

IV. Conclusion

In light of the foregoing, applicants respectfully submit that all claims are in condition for allowance, and an early notification to that effect is earnestly solicited. The examiner is invited to contact the undersigned attorney at (512) 536-3184 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



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